NATIONAL INSTITUTE OF MENTAL HEALTH, NIH
ALFRED E. MANN INSTITUTE FOR BIOMEDICAL ENGINEERING
AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

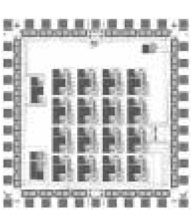
Toward Replacement Parts for the Brain

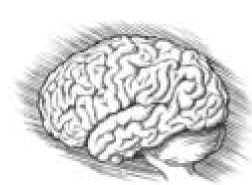
Intracranial Implantation of Hardware Models of Neural Circuitry

Willard Inter-Continental Hotel
Washington DC

August 12-14, 1999

http://www.usc.edu/dept/biomed/NeuralProstheticsCNF/

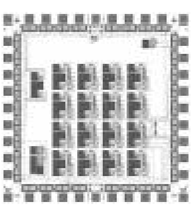


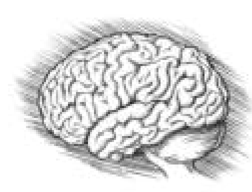


Toward Replacement Parts for the Brain

Intracranial Implantation of Hardware Models of Neural Circuitry

This conference brings together leading researchers throughout the country for a focus on one of the newest frontiers of neuroscientific and bioengineering research: the intracranial implantation of computer chip models of brain circuitry as neural prosthetics to replace damaged or dysfunctional brain tissue. In considering the development of "replacement parts for the brain," speakers will address recent advances in (i) biologically realistic mathematical models of brain or spinal cord function, (ii) silicon- and/or photonics-based computational devices which incorporate those models, and (iii) "neuron-silicon interface" devices, i.e., micron-scale multi-site electrode arrays to provide bi-directional communication between the computational element and functioning neuronal tissue. The conference is intended to synergize interdisciplinary research in the neural, engineering, and biomedical sciences.





Conference Agenda

Thursday, August 12th

CONFERENCE WELCOME AND OVERVIEW

9:00-9:40 Dennis L. Glanzman, NIMH
Richard K. Nakamura, NIMH
David D'Argenio, AMI USC
Theodore W. Berger, USC

SESSION 1 NEURAL PROSTHETICS FOR SENSORY TRANSDUCTION

9:40-10:30 ***We Made the Deaf Hear. Now What?***
Gerald Loeb, Queens University, Canada

10:30-11:20 ***Microelectronic Array for Stimulation of Large Retinal Tissue Areas***
Dean Scribner, Naval Research Laboratory, and
Mark Humayun, Johns Hopkins University

11:20-11:40 Coffee Break

11:40-12:30 ***The Application of High Electrode Count Electrode Arrays in the Central and Peripheral Nervous Systems***
Richard A. Normann, University of Utah

12:30-1:30 Hosted Luncheon

SESSION 2 HARDWARE IMPLEMENTATIONS OF NEURAL NETWORKS

1:30-2:20 ***Hardware Models of Dynamic Synapse Hippocampal Neural Networks***
Theodore W. Berger, University of Southern California

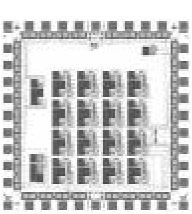
2:20-3:10 ***Listening to Brain Circuits***
Richard Granger, University of California, Irvine

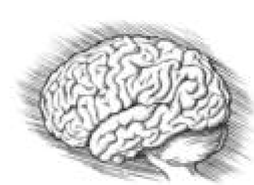
3:10-3:30 Afternoon Coffee Break

3:30-4:20 **Hybrid Electronic/Photonic Multichip Modules for Vision and Neural Prosthetic Applications**
Armand Tanguay, Jr., University of Southern California

4:20-5:00 Discussion

Dinner (on your own)





Conference Agenda

Friday, August 13th

9:00-9:10 Morning Business
Dennis Glanzman, National Institute of Mental Health

SESSION 3 THE NEURON-SILICON INTERFACE

9:10-10:00 ***The Neurochip: A New Multielectrode Device for Stimulating and Recording from Cultured Neurons***
Mike Maher, Aurora Biosciences, Inc.

10:00-10:50 ***Interfacing Nervous System Cells to Solid State Devices***
Harold Craighead, Cornell University

10:50-11:20 Morning Coffee Break

11:20-12:00 ***Long-Term Coupling of Monolayer Neuronal Networks to Multielectrode Arrays in Culture***
Guenter Gross, University of North Texas

12:00-1:15 Lunch (on your own)

SESSION 4 NEURON POPULATION DYNAMICS AND INFORMATION CODING IN THE NERVOUS SYSTEM

1:20-2:10 ***Neural Circuits for Analyzing Auditory Temporal Patterns***
Ellen Covey, University of Washington

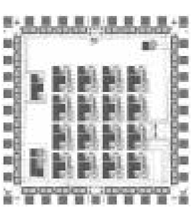
2:10-3:00 ***Rapid Plasticity in Cortical Neuronal Populations.***
Steven P. Wise, National Institute of Mental Health

3:00-3:20 Afternoon Coffee Break

3:20-4:10 ***Information Encoding by Ensembles of Hippocampal Neurons: Dynamics of Representation, Transference and Retrieval***
Samuel Deadwyler, Wake Forest University School of Medicine

4:10-5:00 Discussion

6:30-8:00 Hosted Banquet



Conference Agenda

Saturday, August 14th

9:00-9:10 Morning Business
Theodore W. Berger, University of Southern California

SESSION 5 ADAPTIVE IMPLANT TECHNOLOGY AND IMPLANT-BASED REHABILITATION

9:10-10:00 ***Photonic Artificial-Neural Adaptive Systems with Applications to Vision***
B. Keith Jenkins, University of Southern California

10:00-10:50 ***Optically-Reconfigurable Field-Programmable Gate Array Systems***
José Mumbru, California Institute of Technology

10:50-11:20 Morning Coffee Break

11:20-12:00 ***Toward a Multimedia Approach to Personalized Prosthetics***
Shahram Ghandeharizadeh, University of Southern California

12:00-1:15 Lunch (on your own)

SESSION 6 THE "BUSINESS" OF NEURAL PROSTHESIS TECHNOLOGIES

1:20-2:10 ***The Coming Revolution: Computational Neuroscience and Semiconductor Engineering***
Dan Hammerstrom, Oregon Graduate Institute

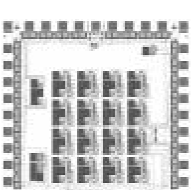
2:10-3:00 ***The "Business" of Implantable Prosthetics for Neurostimulation***
Jeff Greiner, President, Advanced Bionics Corp.

3:00-3:20 Afternoon Coffee Break

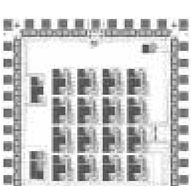
3:20-4:10 ***The Alfred E. Mann Institute for Biomedical Engineering***
David D'Argenio, Interim Director, AMI-USC

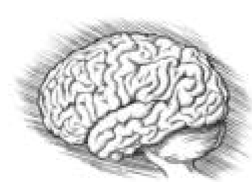
4:10-5:00 Discussion and Meeting Wrap-Up

Dinner (on your own)



Abstracts of Invited Presentations





We Made the Deaf Hear. Now What?

Gerald E. Loeb
Queens University, Kingston, Ontario, Canada

The cochlear prosthesis is one of the most complex feats of biomedical engineering to date. It restores functional levels of speech perception in the large majority of recipients who would otherwise be profoundly or severely deaf. It remains to be seen whether this is now a mature technology capable of only cosmetic improvements or whether breakthrough improvements in function remain to be achieved through systematic neurophysiological research.

The clinical and commercial success of cochlear implants has encouraged neural prosthetic approaches to other sensory, motor and autonomic disorders. Much can be learned from the challenges, failures, and successes of cochlear implants. Some general considerations will be offered for discussion.

Notes:

Microelectronic Array for Stimulation of Large Retinal Tissue Areas

Dean Scribner / Mark Humayun
Naval Research Laboratory / Johns Hopkins University

NRL and JHU are designing and fabricating a very large format retinal stimulator device to be used in human experiments at the Johns Hopkins University, Wilmer Ophthalmological Institute. The initial devices will be used for electrical stimulation of human retinae for short durations in an operating room environment. The aim of the program is to electrically create spatial patterns and temporal sequences on the retina. The JHU group has previously shown that controlled electrical pulses delivered via a single electrode can enable a totally blind patient to see a spot of light. The spot of light spatially corresponds to the retinal area directly under the stimulating electrode. Recently, spatial patterns of electrical stimulation using a 5x5 electrode array have resulted in blind patients seeing very simple shapes. The retina is accessible by an ophthalmologist during surgery and the retinal topography is highly amenable to stimulation using electrode arrays.

The goal of the NRL/JHU project is to create and study a large-scale microelectronic interface with $>10^4$ microelectrodes that will stimulate millions of retinal neurons. The effects will be qualitatively evaluated by the perceptual observations of the human under test. Such a large-scale interface between a microelectronic stimulator and neural tissue is unprecedented. This approach is also novel in that it directly elicits human perceptions rather than recording cellular potentials. It will also give insight into the essence of the image processing functions that are performed by the various neural layers of the retina. The presentation will focus on the device now under development, which uses two recent technologies: (1) nanochannel glass to achieve a high density, conformal interface with the retina; and (2) infrared focal plane array multiplexer designs to achieve a high speed data input with a minimal number of electrical leads.

Notes:

The Application of High Electrode-Count Electrode Arrays in the Central and Peripheral Nervous Systems

Richard A. Normann
University of Utah

Silicon based, high electrode count electrode arrays have been developed in a number of laboratories over the past decade. These devices are intended to be used to acquire basic knowledge regarding parallel processing of information by the nervous system, and, ultimately, as intelligent interfaces that can restore limited function to the damaged or diseased nervous system. The performance specifications of these implant systems in recording from or in stimulating large numbers of neurons in the central and peripheral nervous systems will be discussed. The biocompatibility of these implant systems will also be discussed.

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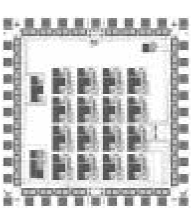

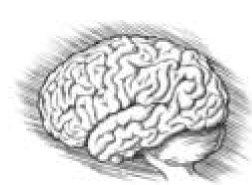

Hardware Models of Dynamic Synapse Hippocampal Neural Networks

Theodore W. Berger
University of Southern California

An effort to develop a technology for hardware implementation of neural network models to be used as neural prostheses for the replacement of damaged or dysfunctional brain tissue will be described. The five components of this effort include (i) experimental study of cellular and molecular mechanisms, (ii) formulation of biologically realistic models of network dynamics, (iii) hardware implementation of the network models in analog VLSI, iv) photonic interconnection of analog VLSI devices for realization of multi-chip modules, and (v) hybrid neuron-silicon devices for interfacing brain implants with existing neural tissue. This five-part approach is applied to developing a prosthetic device for the hippocampus, a region of the brain responsible for the formation of long-term memories, and that frequently is damaged as a result of epilepsy, stroke, and Alzheimer's disease.

The hippocampus is typical of most neural systems found in the mammalian brain in that it is composed of several populations of neurons, each with a distinct set of functional properties that include higher order nonlinearities, and are interconnected through a variety of feedforward and feedback circuits. Because of its special role in memory formation, the strengths of connections between hippocampal neurons also are subject to activity-dependent modification, i.e., the system properties can be nonstationary. In the intact hippocampus, subpopulations of neurons are involved in distributed representations of stimuli and/or behavior that can be altered with changing experience or context. Collectively, these system characteristics present a unique set of challenges to developing a biologically realistic model at the systems level which also provides a sufficient basis for a partial replacement neural prosthetic.

With recent advances in neuroscience, biomedical and electrical engineering, and medicine, we appear to be on the threshold of overcoming many of these challenges with present-day and emerging technologies, to the extent that the first applications of silicon-based computational elements having direct communication with brain tissue may be realized in the near future. Efforts to develop “smart” neural prostheses also are leading to a new generation of “spin-off” technologies that are highly useful for real-world applications, e.g., speech recognition and robotics control systems.

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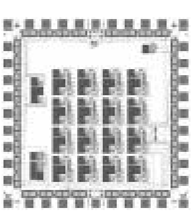

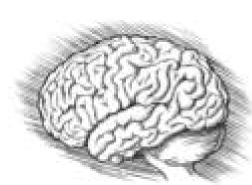

Listening to Brain Circuits

Richard Granger
University of California, Irvine

Silicon neural interfaces can only talk to the brain if they speak its language. Newfound understanding of codes used by peripheral systems (e.g., retina, cochlea) has enabled striking recent advances in prosthetics for the deaf and blind, but for central brain systems (e.g., memory, perception, emotion, navigation) the codes are only beginning to be deciphered. New experimental techniques, from active (immediate-early) gene mapping to novel brain activity assessment devices, illuminate brain circuit function; and new computational systems from sensors to robotics provide testbeds for our ability to duplicate these functions. Recent advances have been achieved in three primary areas: smart sensors, visual navigation by mobile robots, and novel medical diagnostic methods and devices.

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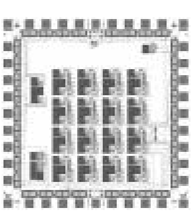

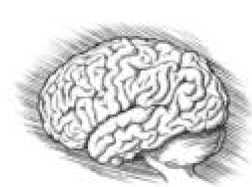

Hybrid Electronic/Photonic Multichip Modules for Vision and Neural Prosthetic Applications

Armand R. Tanguay, Jr.
University of Southern California

Research will be described on the dense interconnection of large-scale arrays of neuron-like units by means of a hybrid electronic/photonic packaging approach. In our approach, multiple layers of silicon VLSI chips are configured with arrays of hybrid analog/digital cells that implement neuron-like functionality, and at the same time contain associated arrays of photodetectors for receiving optical inputs. Individual cells can be electrically interconnected within each layer out to nearest or next nearest neighbors, and are interconnected vertically between layers by means of dense fan-out/fan-in optical/photonic interconnections that extend to higher order nearest neighbors. Such hybrid electronic/photonic multichip modules are conceived to contain upwards of a million neuron units per layer, with approximately a billion weighted interconnections per cubic centimeter, and may provide a step along the road to neural prosthetic devices.

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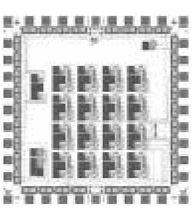

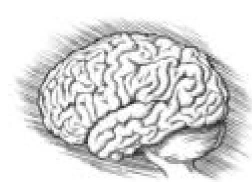

The Neurochip: A New Multielectrode Device for Stimulating and Recording from Cultured Neurons

Mike Maher
Aurora Biosciences, Inc.

The neurochip is a silicon micromachined device upon which cultured mammalian neurons can be continuously and individually monitored and stimulated. The neurochip is based upon a 4x4 array of metal electrodes, each of which has a caged well structure designed to hold a single mature cell body while permitting normal outgrowth of neural processes. This device permits simultaneous, non-invasive, bi-directional communication with individual neurons in self-assembled neuronal networks. Implantable versions of this device may allow the development of a direct interface to the nervous system at the single cell level.

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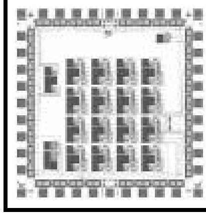

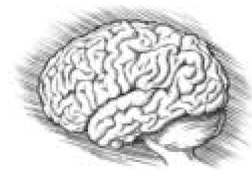

Chemical and Topographical Patterning for Guidance of Central Nervous System Cells in Culture

Harold G. Craighead
Cornell University

This talk will present methods and results for culturing central nervous system cells on inorganic surfaces with patterns of surface chemistry or surface topography. This can be used to guide and organize cells on surfaces and electrode arrays. The patterning techniques include micro-contact printing of high-resolution proteins with alignment to surface features, and etching of micrometer-size and sub-micrometer surface features in silicon substrates. The lithographically generated patterns provide substantial flexibility in the types of surfaces that can be created. Results of culturing of neurons and glial cells and electrical recording from neurons will be discussed.

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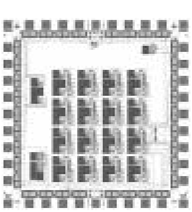

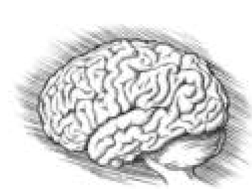

Long-Term Coupling of Monolayer Neuronal Networks to Multielectrode Arrays in Culture

Guenter Gross
University of North Texas

Neuronal networks in culture are accessible to a great variety of experimental methods. If derived from dissociated embryonic CNS tissue, they form shallow three-dimensional cell layers that allow the simultaneous application of the following investigative techniques: (a) multichannel extracellular recording with substrate-integrated microelectrodes, (b) high-power microscopy, (c) precise manipulation of the medium, (d) fluorescence measurements, and (e) electrical stimulation through recording electrodes. Network development, including cell-surface and cell-electrode interactions can be followed with time lapse photography and cell death can be determined quantitatively. These systems are totally accessible pharmacologically and have shown the following important characteristics: continual spontaneous activity, complex burst and spike patterns, high sensitivity to neuroactive or toxic compounds, compound-specific activity pattern changes, tissue-specific responses, and high intra- and interculture reproducibility of pharmacological responses. Although subtle aspects of information processing, which are more dependent on circuit structure, may not be histiotypic in culture, pharmacological responses are robust, highly reproducible, and representative of the parent tissue. Present techniques using a hydrophobic polysiloxane insulation, activated in adhesion islands and decorated with poly-D-lysine and laminin, generate a stable, confluent glial layer (carpet) with neurons on the surface of this carpet and axons both below and above the carpet. Most recordings are obtained from axons. Statistically, cell-electrode coupling in terms of mean and maximum signal-to-noise ratios and number of electrodes active does not decrease with age (up to 6 months). Spike shape changes at individual electrodes, if they occur, are slow, but have not been followed for more than 10 days continuously. The reproducibility of pharmacological responses is also not overtly age dependent. Problems are occasionally seen in culture batches where all networks from a specific preparation date appear inferior and are usually eliminated. Under optimum conditions, networks in culture are highly stable and remain responsive to pharmacological manipulation. Such networks, and the concomitant technology, provide interesting experimental systems that lie between biochemistry and whole animal experiments and provide rapid, quantitative information on neurophysiological responses to chemicals. New pulsed-plasma deposition methods that polymerize allylamines on the polysiloxane substrate have shown promising results and indicate that polylysine and laminin surface decoration might be eliminated.

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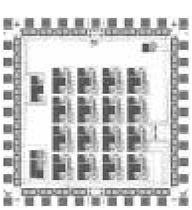

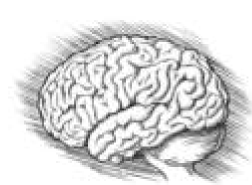

Neural Circuits for Analyzing Auditory Temporal Patterns

Ellen Covey
University of Washington

The central auditory system initially consists of multiple parallel pathways, each of which provides a unique transformation of the physical signal. Each pathway is made up of neurons whose intrinsic properties and connectivity form the basis for these transformations. Convergence of parallel pathways results in neurons tuned to biologically important patterns of sound. This tuning is determined by the temporal relationships among convergent inputs that may be excitatory or inhibitory, with different latencies and time-courses. Using what we know about the temporal dynamics of auditory neural populations, we can construct simple models of the neural circuitry that produces tuning to auditory patterns, and can derive general principles of how neural circuits encode time-varying patterns of information.

Notes:

Rapid Plasticity in Cortical Neuronal Populations

Steven P. Wise
National Institute of Mental Health

Recent neurophysiological research on monkeys has revealed that cortical activity shows remarkable and rapid learning-dependent plasticity. Populations of cortical neurons change their activity levels as monkeys learn arbitrary input-output mappings or adapt to novel sensorimotor transforms. This activity change occurs in a broad population of neurons over the time course of learning, which takes place in minutes. A similar time course is seen for practice-induced plasticity in the motor cortex of humans. After ~30 minutes of practicing thumb movements in a given direction, the movement evoked by stimulation of the motor cortex changes to reflect the practiced direction.

Notes:

Information Encoding by Ensembles of Hippocampal Neurons: Dynamics of Representation, Transference and Retrieval

Samuel Deadwyler
Wake Forest University School of Medicine

Ensembles of hippocampal neurons (mostly CA3 and CA1 cells) are recorded in rats performing a short-term memory (delayed nonmatch to sample-DNMS) task. Multivariate statistical analysis and characterization of single neuron firing patterns during the task mutally support the fact that neurons within the ensemble selectively encode "conjunctions" or combinations of task-relevant attributes. such that information is partitioned and distributed across the entire ensemble in a spatio-temporal manner during critical phases of the task. The spatio-temporal pattern is captured within hippocampus by electrode arrays with fixed recording positions that allow determination of functional as well as anatomic correlates of information transition from the Sample to Delay phases of the task. This accomplished by temporally dependent activation of different "functional types" of neurons within the ensemble in the manner of a categorizing neural net with mutually inhibitory inputs. These "mechanics of memory" or, information processing within hippocampal ensembles, provide a basis for the establishment of realistic algorithms to detect, assess and simulate those same patterns in neural prosthetic applications.

Notes:

Photonic Artificial-Neural Adaptive Systems with Applications to Vision

B. Keith Jenkins
University of Southern California

Advances in optical, photonic, and electronic technologies enable ever more processing and communication power in smaller packages. These advancements make future processing capability per unit volume approaching that of portions of the human brain be considered in circles outside of science fiction. Two scenarios of photonic systems for artificial-neural computation are described, one based on compact 3-D multichip modules and one based on real-time holographic materials. Physically fixed and physically dynamic interconnections in the systems will be contrasted. Some of the potential, limitations, and unresolved issues are discussed.

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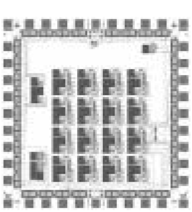

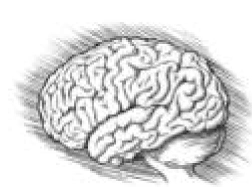

Optically Reconfigurable Field Programmable Gate Array Systems

José Mumbru
California Institute of Technology

Many applications in neural prosthetics can benefit from processors able to reprogram their hardware in order to learn how to perform a given task and with the flexibility of adapting themselves to changes in the environment where such task is performed. The Optically Programmable Gate Array (OPGA), an enhanced version of a conventional Field Programmable Gate Array (FPGA), utilizes a holographic memory accessed by an array of Vertical Cavity Surface Emitting Laser, or VCSELs, to program its logic. Combining spatial and shift multiplexing to store the configuration pages in the memory, the OPGA module is very compact and has extremely short configuration time allowing for dynamic reconfiguration.

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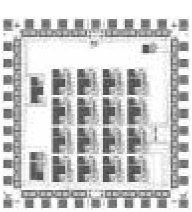

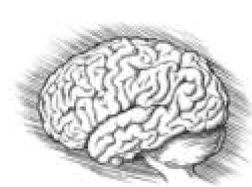

Toward a Multimedia Approach to Personalized Prosthetics

Shahram Ghandeharizadeh
University of Southern California

Advances in computer processing, networks, and storage devices have made multimedia information systems a reality. These systems exercise our senses in support of diverse applications such as physical therapy, training, etc. For example, haptic devices can be employed to enable a patient to experience the capabilities of either a transplant or an artificial limb, e.g., an artificial hand dialing a telephone, using a chopstick, etc. This paper describes the role of haptic devices and multimedia databases in support of physical training. Moreover, it outlines ideas on how historical data can be used to fine-tune either a training process, the artificial limb, or both.

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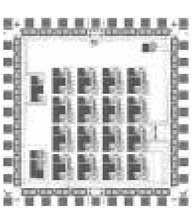

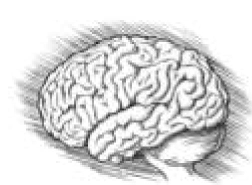

The Coming Revolution:
Computational Neuroscience and Semiconductor Engineering

Dan Hammerstrom
Oregon Graduate Institute

Many believe that the most important result to come out of the last ten years of neural network research is the significant change in perspective in the neuroscience community towards computational neurobiology and functional models. Arriving on a fast moving train from the other direction is semiconductor technology, one of the greatest technology success stories of all time transistors are now approaching deep submicron (less than 100 nanometers) in size, and we will soon be building silicon chips with over 100 million transistors. The marriage of these two technologies is creating what Andy Grove (ex-CEO of Intel) refers to as a strategic inflection point.

Although previous attempts at merging these technologies were premature, it is my belief that silicon and computational neurobiology will soon merge to create an extremely powerful, and radically new form of computation.

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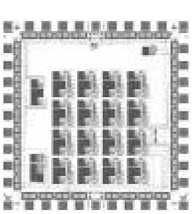

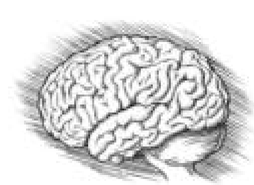

The "Business" of Implantable Prosthetics for Neurostimulation

Jeff Greiner
Advanced Bionics Corporation

There are many potential applications where the use of implantable neurostimulation can resolve or ameliorate neural deficits. These applications include Parkinson's Disease, epilepsy, tremor, blindness, sleep apnea, facial nerve palsy, urinary incontinence, deafness, intractable pain, as well as the movement of paralyzed limbs. A business choice of which application to pursue will depend upon several factors, including: the number of patients who can potentially benefit, the alternative therapies available, the total investment necessary, the reimbursement picture, and the intellectual property in the area. This presentation will describe these factors in order to develop a greater appreciation for the possibilities of collaboration between academia and commerce in the area of neurostimulation.

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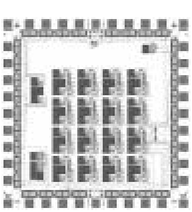

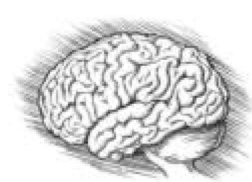

The Alfred E. Mann Institute for Biomedical Engineering

David Z. D’Argenio
Alfred Mann Institute for Biomedical Engineering
University of Southern California

The Alfred E. Mann Institute for Biomedical Engineering at the University of Southern California (AMI-USC) was established in September, 1988 as a non-profit institute engaged in advanced biomedical research, with the goal of fostering the development and commercialization of medical devices and other biomedical technologies to improve human health and well-being. To accomplish this goal, AMI-USC collaborates with USC faculty from engineering, biological sciences, and medical sciences to conduct innovative research leading to the transfer of new technologies to private industry. The AMI-USC was established in 1998 through a $100 million endowment by Alfred E. Mann, one of the country's leading biomedical entrepreneurs. In addition to this endowment, USC will create an environment in which USC faculty and Institute engineers and scientists work collaboratively on the development of biomedical technologies, consisting of a 70,000 sq. ft. facility to house both the Institute and USC's Department of Biomedical Engineering, which is scheduled for opening in 2002. Ultimately, the expansion provided by the AMI-USC endowment will support an additional 8-10 full-time faculty in Biomedical Engineering, 25 faculty and staff within the AMI-USC and other academic departments throughout USC, graduate and postdoctoral fellowship support in biomedical engineering and undergraduate internships through involvement in the Institute's projects. The Institute engages faculty throughout the University to extend research ideas into viable technologies that can be transferred to the medical market place. This talk will discuss the Institute’s organization and its core competencies in neural prostheses and other areas.

Alfred E. Mann was the founder and CEO of Pacesetters, Inc., one of the world's leading manufacturers of cardiac pacemakers, and is currently the President and CEO of MiniMed, Inc., the world's leading manufacturer of microinfusion pumps for the treatment of diabetes and other diseases. Mr. Mann also is the founder and CEO of Advanced Bionics Corp., one of the two leading manufacturers of cochlear implants and a company dedicated to the development of implantable electrical stimulation devices for neural and neuromuscular prostheses, as well as the founder of Second Sight Corp., a recently established company with the goal of developing an artificial retina to restore vision to patients suffering retinal damage and/or degeneration. Through additional entities, the Medical Research Group, Inc., which recently developed the first long-term, implantable glucose sensor for continuous monitoring of glucose levels in diabetics, and the Alfred E. Mann Foundation, Mr. Mann supports research and development of an additional range of biomedical and neural engineering technologies.

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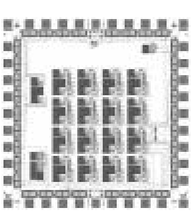
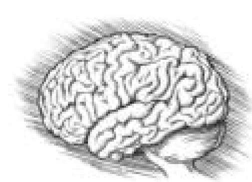




Conference Directors

Theodore W. Berger, Ph.D.
Department of Biomedical Engineering
500 Olin Hall
University of Southern California
Los Angeles, CA 90089-1541
Phone: 213-740-8017
E-mail: berger@bmsrs.usc.edu

Dennis L. Glanzman, Ph.D.
National Institute of Mental Health, NIH
6001 Executive Boulevard
Room 7171, MSC 9637
Bethesda, MD 20892-9637
Phone: 301-443-1576
E-mail: glanzman@helix.nih.gov

Invited Speakers

Ellen D. Covey, Ph.D.
Department of Psychology
323 Guthrie Hall
University of Washington
P.O. Box 351525
Seattle, WA 98195
Phone: 206-616-8112
E-mail: ecovey@u.washington.edu

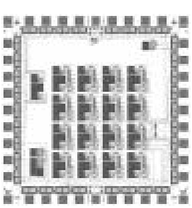
Samuel Deadwyler, Ph.D.
Department Physiology
and Pharmacology
Wake Forest University
Medical Center Boulevard
Winston-Salem, NC 27157
Phone: 336-716-8540
E-mail: sdeadwyl@ddlb.neuro.wfu.edu

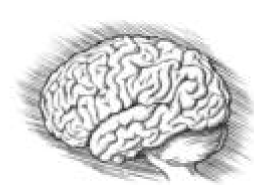
Harold Craighead, Ph.D.
Applied and Engineering Physics
210 Clark Hall
Cornell University
Ithaca, NY 14853-3501
Phone: 607-255-8707
E-mail: hgc1@cornell.edu

Shahram Ghandeharizadeh, Ph.D.
Department of Computer Science
SAL 208
University of Southern California
Los Angeles, CA 90089
Phone: 213-740-4781
E-mail: shahram@pollux.usc.edu

David D'Argenio, Ph.D.
Alfred E. Mann Institute
for Biomedical Engineering, and
Department of Biomedical Engineering
500 Olin Hall
University of Southern California
Los Angeles, CA 90089-1541
Phone: 213-740-0838
E-mail: dargenio@bmsrs.usc.edu

Richard Granger, Ph.D.
Department of Information
and Computer Science
University of California
Irvine, CA 92717-3425
Phone: 949-824-2993
E-mail: granger@ics.uci.edu





Invited Speakers (cont'd.)

Jeff Greiner, President
Advanced Bionics Corporation
12740 San Fernando Road
Sylmar, CA 91342
Phone: 818-362-7588
E-mail: jeffg@advancedbionics.com

Guenter W. Gross, Ph.D.
Center for Network Neuroscience
P.O. Box 305220
Department of Biological Sciences
University of North Texas
Denton, TX 76203
Phone: 940-565-3615
E-mail: gross@nervous.cnns.unt.edu

Dan Hammerstrom, Ph.D.
Department of Electrical and
Computer Engineering
Oregon Graduate Institute
20000 NW Walker Road
Beaverton, OR 97007
Phone: 503-748-4037
E-mail: strom@ece.ogi.edu

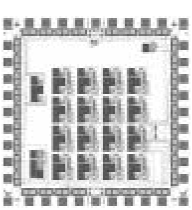
B. Keith Jenkins, Ph.D.
Department of Electrical Engineering
Signal & Image Processing Institute
Electrical Engineering Bldg., 404A
Mail Code 2564
University of Southern California
Los Angeles, CA 90089
Phone: 213-740-4149
E-Mail: jenkins@sipi.usc.edu

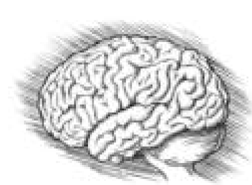
Gerald Loeb, M.D.
Department of Physiology
Queen's University
Rm. 104 Abramsky Hall
Kingston, ON K7L 3N6 CANADA
Phone: 613-533-2790
E-mail: loeb@biomed.queensu.ca

Mike Maher, Ph.D.
Aurora Biosciences Corporation
11010 Torreyana Road
San Diego, CA 92121
Phone: 619-404-6600
E-mail: maherm@aurorabio.com

José Mumbru
Department of Electrical Engineering
California Institute of Technology
Mail Stop 136-93
Pasadena, CA 91125
Phone: 626-395-3888
E-mail: jmumbru@sunoptics.caltech.edu

Richard Norman, Ph.D.
Department of BioEngineering
Joseph Merrill Engineering Building
50 S. Central Campus Drive, Room 2480
University of Utah
Salt Lake City, UT 84112-9202
Phone: 801-581-7645
E-mail: normann@m.cc.utah.edu





Invited Speakers (cont'd.)

Dean Scribner, Ph.D.
Naval Research Laboratory
4555 Overlook Ave. S.W.
Washington, DC 20375
Phone: 202-767-2225
E-mail: scribner@nrl.navy.mil

Armand R. Tanguay, Jr., Ph.D.
Department of Electrical Engineering
Seaver Science Center 520
University of Southern California
Los Angeles, CA 90089
Phone: 213-740-4403
E-mail: atanguay@usc.edu

Steven P. Wise, Ph.D.
Laboratory of Systems Neuroscience
National Institute of Mental Health
49 Convent Drive
Room 49/B1EE17, MSC 4401
Bethesda, MD 20892-4401
Phone: 301-496-1201
E-mail: spw@codon.nih.gov